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## **Creutzfeldt-Jakob disease revealed by a logopenic variant of primary progressive aphasia**

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# Creutzfeldt-Jakob Disease Revealed by a Logopenic Variant of Primary Progressive Aphasia

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## Key Words

Aphasia • Magnetic resonance imaging • Prion disease • Primary progressive aphasia • Dementia

## Abstract

Logopenic aphasia, mainly characterized by word anomia, sentence and phrase comprehension difficulties secondary to phonological loop deficits but relatively preserved single word comprehension and no agrammatism, is one of the 3 main variants of primary progressive aphasia (PPA). We describe the first case of PPA that fulfilled clinical criteria of logopenic aphasia but showed abnormal DWI hyperintensities that were predominant on the left hemisphere and compatible with Creutzfeldt-Jakob disease (CJD). After abnormally long isolated language deficits, the patient rapidly worsened and died. Autopsy performed 18 months after onset of language difficulties confirmed the diagnosis. We therefore advocate performing DWI sequences in any suspicion of PPA in order to rule out CJD.

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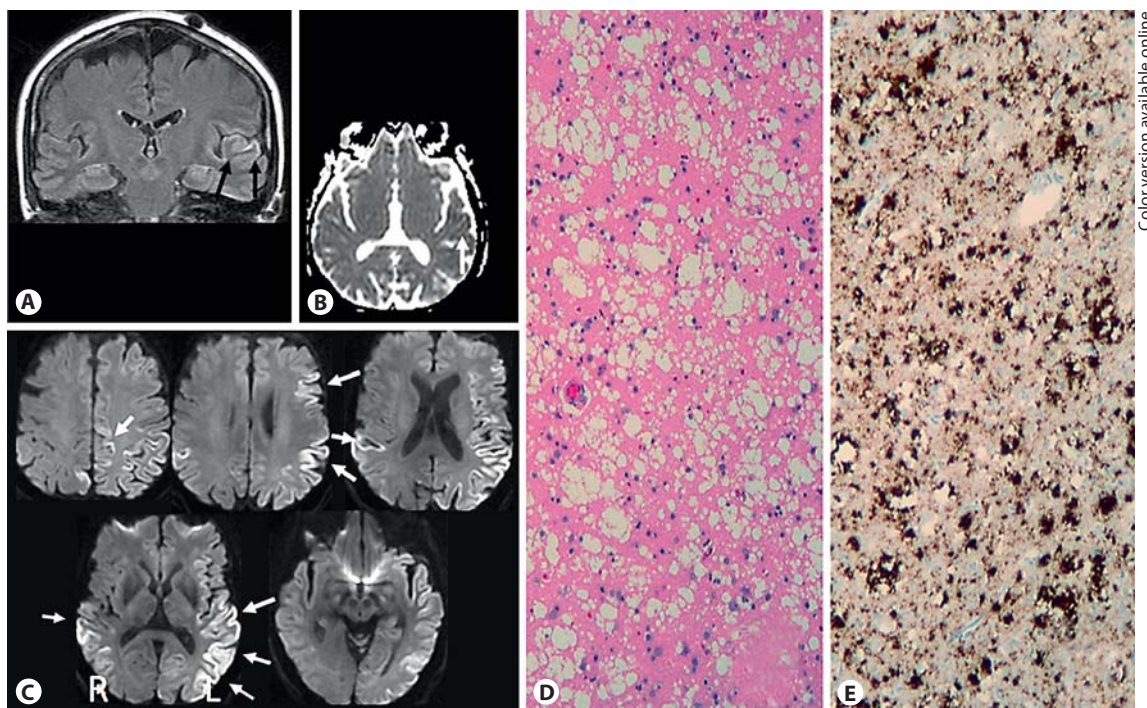
## Introduction

Mesulam was the first to introduce the syndrome of primary progressive aphasia (PPA) in 1982 after observing 6 patients with isolated and progressive language def-

icits caused by a neurodegenerative disease [1]. He also described a fluent and a non-fluent subtype that were characterized by normal articulation, flow and number of words with prominent word comprehension deficits in the former, and decreased mean length of utterance or slow output with agrammatism in the absence of single word comprehension deficits in the latter [2]. Since then, the syndrome of PPA has been a considerable matter of debate and the concept evolved. Recently, an expert panel proposed working research criteria for the 3 main variants of PPA – non-fluent/agrammatic, semantic, and logopenic – including clinical, imaging-supported and pathological diagnostic features [3]. We present a case with the clinical diagnosis of the logopenic variant of PPA but imaging abnormalities compatible with Creutzfeldt-Jakob disease (CJD) that was later confirmed on autopsy.

## Case Description

A 62-year-old right-handed female school teacher started to complain of word finding difficulties in September 2007 that were also noticed by her family, gradually worsened and led to an extensive work-up in March 2008. Neurological examination was entirely normal. Neuropsychological examination showed some disruptions in spontaneous speech fluency with false starts and incomplete sentences, severe word-retrieval anomia in the denomination task (16/34 on the Boston Naming Test) and phonological paraphasias. Repetition of complex words and long sentences was impaired and verbal short-term memory with a digit



**Fig. 1.** **A** FLAIR-weighted sequences showing cortical hyperintensities in the left temporoparietal cortex. **B** Apparent diffusion coefficient showing very equivocal restricted diffusion in the left temporal cortex. **C** DWI-weighted sequences demonstrating unequivocal cortical hyperintensities in the frontal, parietal, and

temporal cortex that are clearly predominant on the left (MRI of March 2008). Histological section of temporal lobe showing **(D)** massive spongiosis of the cortex (H&E staining) with **(E)** abundant prion protein deposits (PrP immunostaining) (autopsy of April 2009).

span of 4 (centile 10). Single word comprehension, writing, reading and semantic knowledge were entirely normal (52/52 for words and pictures on the Pyramid and Palm Tree Test). Episodic memory tested with the French version of the Buschke Memory Impairment Screen (RL-RI 16 item version) was normal when the semantic cue was given (centile 50). The Ray Auditory-Verbal Learning Test and the Ray Visual Design Learning Test scores were also within the normal range (centile 60). The patient performed normally on executive functions assessed with the Stroop and Trail-Making A and B tests. She also scored within the normal range on the Mattis-DRS (139/144, centiles 41–59) and on the Raven Progressive Matrices (centile 40). In March 2008, a routine Brain MRI was performed at our University Hospital. T1-weighted sequences were unremarkable, ADC maps were equivocal, showing an increased coefficient in the left temporal cortex, but FLAIR and unequivocally DWI-weighted sequences revealed abnormal cortical hyperintensities in the frontal, parietal and temporal cortex that were clearly predominant on the left, strongly suggesting CJD (fig. 1) [4–6]. FDG-PET scan found hypometabolism in the left perisylvian region with no deficit in the basal ganglia. Herpes, anti-Hu, anti-Ri, anti-Yo, anti-CV2, amphiphysin, and Ma1 and Ma2 antibodies were negative. Protein 14-3-3 was slightly elevated in the CSF, and A $\beta$ 42 and Tau protein levels were normal. Genetic analysis (codon 129 polymorphism of the PRNP gene) was not performed. EEG was normal. A year after onset of

language difficulties, in September 2008, spontaneous speech was marked with pauses due to worsening of anomia and phonological paraphasias. Phonological loop deficits increased with difficulties in simple word repetition as well as oral naming and oral comprehension. Other domains (executive functions, calculation, episodic memory) were only slightly impaired. MRI abnormalities were moderately larger on both hemispheres, without involvement of basal ganglia. In late November, EEG showed an isolated non-specific slowing in the left frontotemporal regions. In January 2009, she was found with a significant extrapyramidal syndrome on the right with myoclonic jerks and severe dementia. In March 2009, EEG showed typical diffuse periodic lateralized discharges that were more pronounced on the left. She died peacefully at home in April 2009, more than 18 months after the first symptoms of aphasia. Autopsy revealed typical CJD neuropathology (Gambetti type 2 or Collinge type 2/3).

## Discussion

PPA as a primary diagnosis of CJD has been described but clinical details on language findings and the length of the isolated aphasic syndrome have not been reported

[7]. Our patient fulfilled all clinical criteria of the logopenic variant of PPA proposed by PPA experts, i.e. impaired single word retrieval in spontaneous speech and naming, impaired repetition of complex words and sentences, phonological errors in spontaneous speech, spared single word comprehension and object knowledge, spared motor speech and absence of agrammatism [3]. Moreover, imaging-supported diagnosis was also reached with PET findings that showed perisylvian hypometabolism [1]. First, we would suggest to PPA experts to strongly recommend DWI sequences and add it as neuroimaging exclu-

sion criteria. Second, we would like to stress the abnormally long duration of isolated logopenic aphasia in this case that lasted for more than a year before the onset of other suggestive clinical symptoms of CJD. This abnormally long duration matches with a relatively slow neuronal death process reflected by the only slightly elevated 14-3-3 protein and normal Tau levels in the early stage of disease, which is unlike in most cases with CJD where these markers are highly sensitive [8]. Finally, this is the first case of logopenic aphasia with proven CJD neuropathology.

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